

E APPELDOORN/AU 25
L1. 8 S (E1 OR E2 OR E4 OR E5 OR E6 OR E7 OR E8 OR E9 OR E10 OR E11 O
E BIESSEN/AU 25
L2 13 S (E4 OR E5 OR E6 OR E7 OR E8 OR E9 OR E10 OR E11) AND (SELECTI
L3 5 S L2 NOT L1
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L4 0 S (E1 OR E2 OR E4 OR E5 OR E6 OR E7 OR E8 OR E9 OR E10 OR E11 O
E BERKEL/AU 25
L5 0 S (E4 OR E5 OR E6 OR E7 OR E8 OR E9 OR E10 OR E11 OR E12 OR E13
L6 0 S BERKEL/AU

=> fil hcaplus
 COST IN U.S. DOLLARS
 FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
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 FILE LAST UPDATED: 26 Sep 2006 (20060926/ED)

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=> E APPELDOORN/AU 25

E1	1	APPELBY MARK W/AU
E2	1	APPELDOOM CHANTAL C M/AU
E3	0	--> APPELDOORN/AU
E4	6	APPELDOORN CHANTAL C M/AU
E5	4	APPELDOORN CHANTAL CATHARINA MARIA/AU
E6	5	APPELDOORN E/AU
E7	5	APPELDOORN ESTHER/AU
E8	16	APPELDOORN J K/AU
E9	1	APPELDOORN JACQUES WILHELMUS JOZEF/AU
E10	7	APPELDOORN JOHN K/AU
E11	4	APPELDOORN K J/AU
E12	4	APPELDOORN KLAAS J/AU
E13	1	APPELDOORN N J G/AU
E14	2	APPELDOORN NIEK J G/AU
E15	1	APPELDOORN PAUL/AU
E16	1	APPELDOORN RICHARD S/AU
E17	1	APPELDOORN W C A/AU
E18	1	APPELDOORN WM R/AU
E19	4	APPELDORN ROGER H/AU
E20	1	APPELEBEY MALCOLM P/AU
E21	1	APPELET H/AU
E22	1	APPELFELDER B/AU
E23	1	APPELFELDER HEINZ/AU
E24	2	APPELFELDER KLAUS/AU
E25	1	APPELFELLER KLAUS/AU

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1	"APPELBY MARK W"/AU
1	"APPELDOOM CHANTAL C M"/AU
6	"APPELDOORN CHANTAL C M"/AU
4	"APPELDOORN CHANTAL CATHARINA MARIA"/AU
5	"APPELDOORN E"/AU
5	"APPELDOORN ESTHER"/AU
16	"APPELDOORN J K"/AU

1 "APPELDOORN JACQUES WILHELMUS JOZEF"/AU
 7 "APPELDOORN JOHN K"/AU
 4 "APPELDOORN K J"/AU
 4 "APPELDOORN KLAAS J"/AU
 1 "APPELDOORN N J G"/AU
 2 "APPELDOORN NIEK J G"/AU
 1 "APPELDOORN PAUL"/AU
 1 "APPELDOORN RICHARD S"/AU
 1 "APPELDOORN W C A"/AU
 1 "APPELDOORN WM R"/AU
 4 "APPELDORN ROGER H"/AU

9950 SELECTIN

10206 SELECTINS

12453 SELECTIN

(SELECTIN OR SELECTINS)

L1 8 ("APPELBY MARK W"/AU OR "APPELDOOM CHANTAL C M"/AU OR "APPELDOORN CHANTAL C M"/AU OR "APPELDOORN CHANTAL CATHARINA MARIA"/AU OR "APPELDOORN E"/AU OR "APPELDOORN ESTHER"/AU OR "APPELDOORN J K"/AU OR "APPELDOORN JACQUES WILHELMUS JOZEF"/AU OR "APPELDOORN JOHN K"/AU OR "APPELDOORN K J"/AU OR "APPELDOORN KLAAS J"/AU OR "APPELDOORN N J G"/AU OR "APPELDOORN NIEK J G"/AU OR "APPELDOORN PAUL"/AU OR "APPELDOORN RICHARD S"/AU OR "APPELDOORN W C A"/AU OR "APPELDOORN WM R"/AU OR "APPELDORN ROGER H"/AU) AND (SELECTIN)

=> DIS L1 1 IBIB IABS

THE ESTIMATED COST FOR THIS REQUEST IS 2.74 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1 ANSWER 1 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1131240 HCPLUS

DOCUMENT NUMBER: 142:329352

TITLE: Gallic Acid Antagonizes P-Selectin-Mediated Platelet-Leukocyte Interactions

AUTHOR(S): Appeldoorn, Chantal C. M.; Bonnefoy, Arnaud; Lutters, Bianca C. H.; Daenens, Kim; van Berkel, Theo J. C.; Hoylaerts, Marc F.; Biessen, Erik A. L.

CORPORATE SOURCE: Division of Biopharmaceutics, Leiden/Amsterdam Center for Drug Research, Gorlaeus Laboratories, Leiden University, Leiden, Neth.

SOURCE: Circulation (2005), 111(1), 106-112
CODEN: CIRCAZ; ISSN: 0009-7322PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

ABSTRACT:
 Background: Current paradigm attributes the low incidence of cardiovascular disorders in Mediterranean countries despite a high saturated fat intake, the "French paradox," to the antioxidant capacity of red wine polyphenols. Conceivably, other antiinflammatory pathways may contribute to at least a similar extent to the atheroprotective activity of these polyphenols. We have investigated whether gallic acid (GA), an abundant red wine polyphenol, modulates the activity of P-selectin, an adhesion mol. that is critically involved in the recruitment of inflammatory cells to the vessel wall and thus in atherosclerosis. Methods and Results: GA potently inhibited the binding of a peptide antagonist (IC50, 7.2 μ mol/L) and biotin-PAA-Lea-SO3H, an established high-affinity ligand, to P-selectin (IC50, 85 μ mol/L). Under dynamic flow conditions, GA markedly and dose dependently attenuated the rolling of monocytic HL60 cells over P-selectin-transfected Chinese hamster ovary cells (EC50, 14.5 μ mol/L) while increasing the velocity of P-selectin-dependent rolling of human blood leukocytes over a platelet monolayer. In vivo tests established that GA administration to normolipidemic C57/B16 and aged atherosclerotic apolipoprotein E-deficient mice impaired the baseline rolling of conjugates between activated platelets and circulating monocytes over femoral vein endothelium, as judged by online video microscopy (ED50, 1.7 \pm 0.3 and 1.5 \pm 0.4 mg · kg⁻¹ · h⁻¹, resp.). Conclusions: Our findings

provide a solid mechanistic foundation through which GA intervenes in major inflammatory pathobiologies by binding and antagonizing P-selectin.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> DIS L1 2- IBIB TABS

YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):Y

THE ESTIMATED COST FOR THIS REQUEST IS 19.18 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1 ANSWER 2 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1035016 HCPLUS

DOCUMENT NUMBER: 142:11573

TITLE: P-selectin targeting compositions containing
P-selectin targeting peptides conjugated
with lipids

INVENTOR(S): Appeldoorn, Chantal Catharina Maria;
Biessen, Erik Anna Leonardus; Van Berkel, Theodorus
Josephus Cornelis

PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co. Ltd., Japan

SOURCE: Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1481683	A1	20041201	EP 2003-12123	20030530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CA 2527438	AA	20041209	CA 2004-2527438	20040601
WO 2004105783	A1	20041209	WO 2004-EP5873	20040601
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1638588	A1	20060329	EP 2004-735558	20040601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRIORITY APPLN. INFO.:			EP 2003-12123	A 20030530
			WO 2004-EP5873	W 20040601

OTHER SOURCE(S): MARPAT 142:11573

ABSTRACT:

P-selectin targeting ligand mols. are provided as well as compns., including kits, which comprise such P-selectin targeting ligand mols., such composition being useful for use as pharmaceutical formulations which can be administered safely and effectively and as diagnostic formulations. For example, a P-selectin targeting ligand was prepared by reacting N-hydroxysuccimidyl PEG distearoyl phosphatidyl ethanolamine with human P-***selectin*** binding peptide of H2N-DVEWVCVSY-COOH and was incorporated into liposome compns. for P-selectin targeting delivery.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:1035013 HCPLUS
 DOCUMENT NUMBER: 141:420488
 TITLE: Use of polyhydroxy phenols and polyphenols for modulating P-selectin activity
 INVENTOR(S): Biessen, Erik Anna Leonardus; Appeldoorn, Chantal Catharina Maria; Bonnefoy, Arnaud; Van Berkel, Theodorus Josephus Cornelis; Kuiper, Johan; Hoylaerts, Marc Florimond
 PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co. Ltd., Japan
 SOURCE: Eur. Pat. Appl., 13 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1481669	A1	20041201	EP 2003-12122	20030530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CA 2527141	AA	20041209	CA 2004-2527141	20040507
WO 2004105740	A1	20041209	WO 2004-EP4898	20040507
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1651200	A1	20060503	EP 2004-731590	20040507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRIORITY APPLN. INFO.:			EP 2003-12122	A 20030530
			EP 2004-75320	A 20040203
			EP 2004-75545	A 20040219
			EP 2004-75630	A 20040227
			WO 2004-EP4898	W 20040507

ABSTRACT:

The use of polyhydroxy phenols and polyphenols for the manufacture of a medicament for the prevention, treatment or diagnosis of a disease or a condition, wherein P-selectin is involved, is provided. Further, pharmaceutical and nutraceutical compns. which are useful in the diagnosis, prevention, or treatment of diseases and conditions associated with P-selectin activity are provided. Also the use of polyhydroxy phenols and polyphenols as targeting tools to P-selectin expressing cells or tissues in a composition, further comprising an active compound in a vehicle, is provided.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:749799 HCPLUS
 DOCUMENT NUMBER: 141:306913
 TITLE: Blocking endothelial adhesion molecules: a potential therapeutic strategy to combat atherogenesis
 AUTHOR(S): Lutters, Bianca C. H.; Leeuwenburgh, Michiel A.; Appeldoorn, Chantal C. M.; Molenaar, Tom J. M.; Van Berkel, Theo J. C.; Biessen, Erik A. L.

CORPORATE SOURCE: Division of Biopharmaceutics, Leiden/Amsterdam Center for Drug Research, Leiden University, Leiden, Neth.
 SOURCE: Current Opinion in Lipidology (2004), 15(5), 545-552
 CODEN: COPLEU; ISSN: 0957-9672
 PUBLISHER: Lippincott Williams & Wilkins
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English
 ABSTRACT:

Purpose of review: This review provides a concise update of the involvement of endothelial adhesion mols. in atherogenesis, an overview of current advances in the development of adhesion mol. blocking agents, as well as an insight into the potential of these mols. in cardiovascular therapy. Recent findings: As endothelial adhesion mols. are deemed to play an important role in the development and progression of atherosclerotic lesions, they are interesting targets for therapeutic intervention in this process. In particular, P-***selectin*** and vascular cell adhesion mol. 1 are widely considered to hold promise in this regard. Current research efforts center on the design of agents that directly block the interaction of the receptor with its ligand (e.g. soluble P-selectin glycoprotein ligand 1, blocking antibodies, EWVD-based peptides) or that interfere with their synthesis (e.g. antisense oligonucleotides) or their regulatory control by nuclear factor kappa B or peroxisome proliferator-activated receptor gamma. Furthermore, adhesion mols. have been exploited as a target for the specific delivery of drug carriers (e.g. biodegradable particles with entrapped dexamethasone) or therapeutic compds. (e.g. dexamethasone) to the plaque. All approaches have been shown to be effective in blocking adhesion mol. function in in-vitro studies and in-vivo models for inflammation or atherosclerosis. Summary: Although the field has achieved considerable progress in recent years, leading to the development of a number of interesting leads, final proof of their efficacy in cardiovascular therapy is eagerly awaited.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:333730 HCAPLUS
 DOCUMENT NUMBER: 140:332537
 TITLE: Glucose-based compounds with affinity to P-selectin
 INVENTOR(S): Appeldoorn, Chantal Catharina Maria;
 Biessen, Erik Anna Leonardus; Molenaar, Thomas Jacobus
 Maria; Van Berkel, Theodorus Josephus Cornelis
 PATENT ASSIGNEE(S): Yamanouchi Europe B.V., Neth.
 SOURCE: PCT Int. Appl., 28 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033473	A1	20040422	WO 2003-EP11457	20031013
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2501842	AA	20040422	CA 2003-2501842	20031013
AU 2003278090	A1	20040504	AU 2003-278090	20031013

EP 1549658	A1	20050706	EP 2003-769400	20031013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015231	A	20050823	BR 2003-15231	20031013
JP 2006503876	T2	20060202	JP 2004-542495	20031013
US 2005261207	A1	20051124	US 2005-530601	20050407
PRIORITY APPLN. INFO.:				
EP 2002-79232 A 20021011				
WO 2003-EP11457 W 20031013				

OTHER SOURCE(S): MARPAT 140:332537

ABSTRACT:

The invention relates to certain glucose-based compds. with affinity to P-***selectin*** to act as antagonists or partial antagonists of P-***selectin.*** These compds. are useful as targeting ligands with an ability to target drugs and genetic material to cells and tissues expressing P-***selectin.*** The synthesis of glucose-based compds. and their use for the preparation of pharmaceutical compns. for the treatment of P-selectin-associated disorders, the conjugates, pharmaceutical carriers and drug delivery systems comprising these compds., and a method for determining whether a compound is capable of binding to P-selectin are also described.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:182904 HCAPLUS
 DOCUMENT NUMBER: 140:247103
 TITLE: Peptide derivatives binding to P-selectin for diagnostic and therapeutic use
 INVENTOR(S): Appeldoorn, Chantal Catharina Maria;
 Biessen, Erik Anna Leonardus; Molenaar, Thomas Jacobus
 Maria; Kuiper, Johan; Van Berkel, Theodorus Josephus
 Cornelis
 PATENT ASSIGNEE(S): Yamanouchi Europe B.V., Neth.
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018502	A1	20040304	WO 2003-EP7260	20030704
WO 2004018502	C1	20050512		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2493471	AA	20040304	CA 2003-2493471	20030704
AU 2003250899	A1	20040311	AU 2003-250899	20030704
EP 1527086	A1	20050504	EP 2003-792179	20030704
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013019	A	20050712	BR 2003-13019	20030704
JP 2006513141	T2	20060420	JP 2004-530000	20030704
PRIORITY APPLN. INFO.:				
EP 2002-78308 A 20020809				
WO 2003-EP7260 W 20030704				

OTHER SOURCE(S): MARPAT 140:247103

ABSTRACT:

The invention discloses derivs. of compds. which bind selectively to the adhesion mol. human P-selectin, and particularly to such derivs. which comprise a peptide moiety or a functional equivalent of said peptide moiety. In addition, the invention discloses methods for preparing such compds., the use of such compds. in therapeutic or diagnostic methods and in pharmaceutical compns., binding mols. binding to the compds., and a method for determining whether a compound is capable of binding to P-selectin.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:204781 HCPLUS

DOCUMENT NUMBER: 139:78430

TITLE: Rational Optimization of a Short Human P-selectin-binding Peptide Leads to Nanomolar Affinity Antagonists

AUTHOR(S): Appeldoorn, Chantal C. M.; Molenaar, Tom J. M.; Bonnefoy, Arnaud; Van Leeuwen, Steven H.; Vandervoort, Petra A. H.; Hoylaerts, Marc F.; Van Berkel, Theo J. C.; Biessen, Erik A. L.

CORPORATE SOURCE: Gorlaeus Laboratories, Leiden/Amsterdam Center for Drug Research, Division of Biopharmaceutics, Leiden University, Leiden, 2300 RA, Neth.

SOURCE: Journal of Biological Chemistry (2003), 278(12), 10201-10207

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:78430

ABSTRACT:

P-selectin plays an important role in the development of various diseases, including atherosclerosis and thrombosis. In our laboratory we recently identified a number of specific human P-selectin-binding peptides containing a Glu-Trp-Val-Asp-Val consensus motif, displaying a low micromolar affinity for P-selectin ($IC_{50} = 2 \mu M$). In search of more potent antagonists for P-selectin, we have optimized the EWVDV pentapeptide core motif via a two-step combinatorial chemical approach. A dedicated library of peptide derivs. was generated by introducing seven substituents at the N and C termini of the motif. In particular, pentapeptides with gallic acid or 1,3,5-benzenetricarboxylic acid substituents at the N terminus proved to be considerably more potent inhibitors of P-selectin binding than the parental peptide. After removal of the N-terminal glutamic acid from the core sequence, which appeared to be replaceable by a carboxamide function without loss of affinity, a second library was synthesized to map the chemical moieties within the gallic acid or 1,3,5-benzenetricarboxyl acid groups responsible for the enhanced P-selectin binding. Moreover, by varying the length and rigidity of the connective spacer, we have further optimized the spatial orientation of the N-terminal substituent. The combined use of phage display and subsequent combinatorial chemical led to the design of a number of gallic acid-containing peptides with low nanomolar affinity for P-selectin both under static and dynamic conditions ($IC_{50} = 15.4 \text{ nM}$). These small synthetic antagonists, which are equally as potent as the natural ligand P-***selectin*** glycoprotein ligand-1, are promising leads in anti-atherothrombotic therapy.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 8 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:876578 HCPLUS

DOCUMENT NUMBER: 138:318071

TITLE: Specific inhibition of P-selectin-mediated

cell adhesion by phage display-derived peptide antagonists

AUTHOR(S): Molenaar, Tom J. M.; Appeldoom, Chantal C. M.; de Haas, Sonja A. M.; Michon, Ingrid N.; Bonnefoy, Arnaud; Hoylaerts, Marc F.; Pannekoek, Hans; van Berkel, Theo J. C.; Kuiper, Johan; Biessen, Erik A. L. Division of Biopharmaceutics, Leiden/Amsterdam Center for Drug Research, Leiden University, Leiden, 2300 RA, Neth.

CORPORATE SOURCE: SOURCE: Blood (2002), 100(10), 3570-3577

CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

P-selectin is a leukocyte adhesion receptor expressed on activated vascular endothelium and platelets that mediates leukocyte rolling and attachment. Because P-selectin is critically involved in inflammation, we used phage display libraries to identify P-selectin-specific peptides that might interfere with its proinflammatory function. Isolated phage contained a highly conserved amino acid motif. Synthetic peptides showed calcium-dependent binding to P-selectin, with high selectivity over E-selectin and L-selectin. The peptides completely antagonized adhesion of monocyte-derived HL60 cells to P-***selectin*** and increased their rolling velocities in flow chamber expts. Peptide truncation and alanine-scanning studies indicated that an EWVDV (single-letter amino acid codes) consensus motif sufficed for effective inhibition. Intriguingly, the apparent avidity of the peptides was increased 200-fold when presented in a tetrameric form (2 μ M vs. 10 nM), which is consistent with the proposed divalent interaction of P-selectin glycoprotein ligand 1 (PSGL-1) with P-selectin. As the EWVDV peptides inhibit the binding of an established glycoside ligand for P-***selectin*** (sulfated Lewis A), it is conceivable that EWVDV interacts with or in close proximity to the actual carbohydrate recognition domain of P-***selectin***, without being a direct structural mimic of sialyl Lewisx. These ligands are among the most potent antagonists of P-selectin yet designed. Their high affinity, selectivity, and accessible synthesis provide a promising entry to the development of new anti-inflammatory therapeutics and might be a powerful tool to provide important information on the binding site of P-selectin.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'HCAPLUS' ENTERED AT 12:49:29 ON 27 SEP 2006
E APPELDOORN/AU 25

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 E24 1 BIESSY MONE/AU
 E25 1 BIEST D K/AU

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 10206 SELECTINS
 12453 SELECTIN
 (SELECTIN OR SELECTINS)

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=> s 12 NOT 11

L3 5 L2 NOT L1

=> d ibib

L3 ANSWER 1 OF 5 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:698093 HCPLUS
 TITLE: Fibrin and activated platelets cooperatively guide
 stem cells to a vascular injury and promote
 differentiation towards an endothelial cell phenotype
 AUTHOR(S): de Boer, H. C.; Verseyden, C.; Ulfman, L. H.;
 Zwaginga, J. J.; Bot, I.; Biessen, E. A.;
 Rabelink, T. J.; van Zonneveld, A. J.
 CORPORATE SOURCE: Department of Nephrology, Leiden University Medical
 Center, Leiden, Neth.
 SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology
 (2006), 26(7), 1653-1659
 CODEN: ATVBFA; ISSN: 1079-5642
 PUBLISHER: Lippincott Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib 2-5

L3 ANSWER 2 OF 5 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:301483 HCPLUS
 DOCUMENT NUMBER: 142:427737
 TITLE: SDF-1 α /CXCR4 Axis Is Instrumental in Neointimal
 Hyperplasia and Recruitment of Smooth Muscle
 Progenitor Cells

AUTHOR(S): Zernecke, Alma; Schober, Andreas; Bot, Ilze; von Hundelshausen, Philipp; Liehn, Elisa A.; Moepps, Barbara; Mericskay, Mathias; Gierschik, Peter; Biessen, Erik A.; Weber, Christian

CORPORATE SOURCE: Departments of Molecular Cardiovascular Research and Cardiology, Rheinisch-Westfaelische Technische Hochschule, Aachen, Germany

SOURCE: Circulation Research (2005), 96(7), 784-791

CODEN: CIRUAL; ISSN: 0009-7330

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:1059154 HCAPLUS
 DOCUMENT NUMBER: 142:33022
 TITLE: Polyhydroxy phenols and their use in binding P-selectin
 INVENTOR(S): Biessen, Erik Anna Leonardus; Appledoorn, Chantal Catharina Maria; Bonnefoy, Arnaud; Van Berkel, Theodorus Josephus Cornelis; Kuiper, Johan; Hoylaerts, Marc Florimond
 PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 58 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004105740	A1	20041209	WO 2004-EP4898	20040507
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1481669	A1	20041201	EP 2003-12122	20030530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CA 2527141	AA	20041209	CA 2004-2527141	20040507
EP 1651200	A1	20060503	EP 2004-731590	20040507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRIORITY APPLN. INFO.:			EP 2003-12122	A 20030530
			EP 2004-75320	A 20040203
			EP 2004-75545	A 20040219
			EP 2004-75630	A 20040227
			WO 2004-EP4898	W 20040507

OTHER SOURCE(S): MARPAT 142:33022
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:669214 HCAPLUS
 DOCUMENT NUMBER: 139:321339

TITLE: P-selectin as a candidate target in
 atherosclerosis
 AUTHOR(S): Molenaar, Tom J. M.; Twisk, Jaap; de Haas, Sonja A.
 M.; Peterse, Niels; Vogelaar, Bram J. C. P.; van
 Leeuwen, Steven H.; Michon, Ingrid N.; van Berkel,
 Theo J. C.; Kuiper, Johan; Biessen, Erik A. L.
 CORPORATE SOURCE: Leiden/Amsterdam Center for Drug Research, Division of
 Biopharmaceutics, Leiden University, Leiden, 2300 RA,
 Neth.
 SOURCE: Biochemical Pharmacology (2003), 66(5), 859-866
 CODEN: BCPCA6; ISSN: 0006-2952
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:172976 HCAPLUS
 DOCUMENT NUMBER: 138:215255
 TITLE: Peptide compounds selectively binding to P-
 selectin and their therapeutic use
 INVENTOR(S): Molenaar, Thomas Jacobus Maria; Kuiper, Johan; Van
 Berkel, Theodorus Josephus Cornelis; Biessen,
 Erik Anna Leonardus
 PATENT ASSIGNEE(S): Yamanouchi Europe B.V., Neth.
 SOURCE: Eur. Pat. Appl., 13 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1288222	A1	20030305	EP 2001-203314	20010903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2459230	AA	20030313	CA 2002-2459230	20020828
WO 2003020753	A1	20030313	WO 2002-NL566	20020828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1423413	A1	20040602	EP 2002-758940	20020828
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BR 2002012219	A	20040921	BR 2002-12219	20020828
CN 1549824	A	20041124	CN 2002-817193	20020828
JP 2005501544	T2	20050120	JP 2003-525023	20020828
ZA 2004000956	A	20050418	ZA 2004-956	20040205
NO 2004000905	A	20040526	NO 2004-905	20040302
US 2005004035	A1	20050106	US 2004-488509	20040302
PRIORITY APPLN. INFO.:			EP 2001-203314	A 20010903
			WO 2002-NL566	W 20020828

OTHER SOURCE(S): MARPAT 138:215255
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'HCAPLUS' ENTERED AT 12:49:29 ON 27 SEP 2006

E APPELDOORN/AU 25

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L3 5 S L2 NOT L1

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9950 SELECTIN
 10206 SELECTINS
 12453 SELECTIN

(SELECTIN OR SELECTINS)

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PIETER"/AU OR "MOLENAAR ANDRE A A"/AU OR "MOLENAAR ANTON JOHAN"/AU OR

"MOLENAAR ARIAN"/AU OR "MOLENAAR ARNO A"/AU OR "MOLENAAR B"/AU OR "MOLENAAR BERNARD"/AU OR "MOLENAAR BIBI"/AU OR "MOLENAAR BONNIE"/AU OR "MOLENAAR C"/AU OR "MOLENAAR

R C M"/AU OR "MOLENAAR C M T"/AU OR "MOLENAAR CHRIS"/AU OR "MOLENAAR CONSTANCE"/AU OR "MOLENAAR CONSTANCE M T"/AU) AND (SELECTIN)

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- 1 "BERKEL RUEDIGER"/AU
- 1 "BERKEL T J C"/AU
- 1 "BERKEL THEO J C V"/AU

9950 SELECTIN